REMARKS

Claims 49, 57, 58 and 79-81 were pending in the subject application, with claims 1-48, 50-56 and 59-78 having previously been canceled, without prejudice or disclaimer. By this Amendment, claims 49 and 57 have been amended to clarify the claimed subject matter and new claim 82 has been added. Support for the claim amendments can be found in the application as originally filed, for example, at page 12, line 30 through page 13, line 10, page 32, lines 23-35, Figure 9 and the corresponding discussion in the specification on page 33, lines 4-10. Accordingly, Applicant respectfully requests that this Amendment be entered. Claims 49, 57, 58 and 79-82 would be pending upon entry of this amendment, with claims 49 and 82 being in independent form.

Non-statutory Obviousness-Type Double Patenting Rejections

In section 4 of the May 27, 2011 Office Action, claims 49, 57, 58 and 79-81 were rejected as purportedly unpatentable over claims 1-46 of US 6,017,696 (Heller '696) in view of Cozzette et al. (US 5,063,081). In section 5 of the May 27, 2011 Office Action, claims 49, 57, 58 and 79-81 were rejected as purportedly unpatentable over claims 1-46 of US 6,048,690 (Heller '690) in view of Cozzette. In section 6 of the May 27, 2011 Office Action, claims 49, 57, 58 and 79-81 were rejected as purportedly unpatentable over claims 1-37 of US 5,849,486 (Heller '486) in view of Cozzette. In section 7 of the May 27, 2011 Office Action, claims 49, 57, 58 and 79-81 were rejected as purportedly unpatentable over claims 1-8 of US 7,582,421 (Sosnowski) in view of Cozzette.

Applicant respectfully submits that the present application is allowable over the cited references (including the cited claims

of Heller '696, Heller '690, Heller '486 and Sosnowski), for at least the reason that the cited references do not disclose or suggest various aspects of the present application, such as, for example, (i) ***subjecting said individually selected microscopic locations to an electric field prior to hybridization*** and contacting said sample oligonucleotide sequence with said one or more anchor sequences thereby allowing said sample oligonucleotide sequence to hybridize to said one or more anchor (independent claim 49), and (ii) forming a plurality of individually electronically addressable microscopic locations on a substrate, each microscopic location comprising a micro-electrode, and ***said sample oligonucleotide sequence is free to move and be transported between said microscopic locations on said substrate*** (independent claim 82).

Heller '690

Claims 1-46 of Heller '690, as understood by applicant, are directed to a method of hybridization analysis wherein a hybridization product is formed and subjected to a varying electric field force and then the fluorescence thereof is monitored. As described for example in column 9, lines 39-44 of Heller '690, a method of electronic perturbation disclosed in the patent relates to a rise in fluorescence intensity that occurs during electronic dehybridization.

However, claims 1-46 of Heller '690 (reproduced below) are silent regarding the aforementioned aspects (i) and (ii).

> 1. A method for hybridization analysis of a sample, the analysis utilizing an electronic stringency control device, comprising the steps of:
>
> providing the sample, a first probe with a fluorescent label and a second probe with a label under hybridization conditions on the electronic stringency control device,

forming a hybridization product, the hybridization product being attached to the electronic stringency control device,

subjecting the hybridization product to a varying electric field force,

simultaneously monitoring the fluorescence from the hybridization product, and analyzing the fluorescent signal.

2. The method for hybridization analysis of claim 1 wherein the fluorescence is analyzed for the fluorescent perturbation value.

3. The method for hybridization analysis of claim 2 wherein the fluorescence perturbation value is measured for the onset value.

4. The method for hybridization analysis of claim 2 wherein the fluorescence perturbation value is measured for its peak height.

5. The method for hybridization analysis of claim 2 wherein the fluorescence perturbation value is measured for its amplitude.

6. The method for hybridization analysis of claim 2 wherein the fluorescence perturbation value is measured for the slope.

7. The method for hybridization analysis of claim 2 wherein the fluorescence perturbation value is measured for its frequency.

8. The method for hybridization analysis of claim 2 wherein the fluorescence perturbation value is a measure of the rehybridization rate.

9. The method for hybridization analysis of claim 1 wherein the fluorescence is analyzed for the power level of the perturbation.

10. The method for hybridization analysis of claim 1 further including the steps of:

determining a second measure of hybridization between the sample and the probe, and

combining the information obtained by the first analysis including the step of subjecting the hybridization

product to the varying electrophoretic force in the second measure to provide a indication of hybridization.

11. The method for hybridization analysis of claim 10 wherein the second measure of hybridization includes determination of the electronic melting point.

12. The method for hybridization analysis of claim 1 wherein the fluorescent label is placed in proximity to an initial denaturation site, a destabilization site or a site with one or more base mismatch sites.

13. The method for hybridization analysis of claim 12 wherein the fluorescent label is intercalated adjacent a single based mismatch site.

14. The method for hybridization analysis of claim 13 wherein the fluorescent label is ethidium bromide.

15. The method for hybridization analysis of claim 13 wherein the fluorescent label is acridine.

16. The method for hybridization analysis of claim 1 wherein the electrophoretic force is in an amount less than is necessary to effect complete dehybridization of the sample and the probe.

17. The method for hybridization analysis of claim 1 wherein the hybridization product is subject to an oscillating electrophoretic force.

18. The method for hybridization analysis of claim 1 wherein the electric field is a DC field.

19. The method for hybridization analysis of claim 1 wherein the electric field is an AC field.

20. The method for hybridization analysis of claim 1 wherein the electric field is sufficient to provide electrophoretic propulsive force.

21. The method for hybridization analysis of claim 1 wherein at least one label is a fluorophore.

22. The method for hybridization analysis of claim 1 wherein the fluorphore is a donor.

23. The method for hybridization analysis of claim 1

wherein at least one label is chromophore.

24. The method for hybridization analysis of claim 1 wherein the chromophore is a quencher.

25. The method for hybridization analysis of claim 1 wherein the electric field is pulsed.

26. The method for hybridization analysis of claim 25 wherein the pulse comprising a single pulse.

27. The method for hybridization analysis of claim 25 wherein the pulse comprises multiple pulses.

28. A method for achieving electronic fluorescence perturbation on an electronic stringency control device comprising the steps of:

locating a first polynucleotide and a second polynucleotide adjacent the electronic stringency control device, the first polynucleotide and second polynucleotide being complementary over at least a portion of their lengths and forming a hybridization product, the hybridization product being attached to the electronic stringency control device, the hybridization product having an associated environmentally sensitive emissive label,

subjecting the hybridization product and label to a varying electrophoretic force,

monitoring the emission from the label, and

analyzing the monitored emission to determine the electronic fluorescence perturbation effect.

29. The method for hybridization analysis of claim 28 wherein the electric field is a DC field.

30. The method for hybridization analysis of claim 28 wherein the electric field is an AC field.

31. The method for hybridization analysis of claim 28 wherein the electric field provides electrophoretic force.

32. The method for hybridization analysis of claim 28 wherein the label is a fluorophore.

33. The method for hybridization analysis of claim 28 wherein the fluorphore is a donor.

34. The method for hybridization analysis of claim 28 wherein the label is a chromophore.

35. The method for hybridization analysis of claim 28 wherein the chromophore is a quencher.

36. The method for hybridization analysis of claim 28 wherein the electric field is pulsed.

37. The method for hybridization analysis of claim 36 wherein the pulse comprising a single pulse.

38. The method for hybridization analysis of claim 36 wherein the pulse comprises multiple pulses.

39. The method for achieving electronic fluorescence perturbation of claim 28 wherein the label is a fluorophore.

40. The method for achieving electronic fluorescence perturbation of claim 28 wherein the label is a chromophore.

41. The method for achieving electronic fluorescence perturbation of claim 28 wherein the label is located within 0 to 10 bases of a base mismatch site.

42. The method for achieving electronic fluorescence perturbation of claim 28 wherein the label is located within 0 to 5 bases of a base mismatch site.

43. A method for distinguishing a match and a mismatch between a target and a probe utilizing an electronic stringency control device, comprising the steps of:

providing a hybridization product including the sample, probe and radiation emissive label adjacent the electronic stringency control device, the hybridization product being attached to the electronic stringency control device,

subjecting the hybridization product to an electronically stringent condition,

monitoring the radiation emitted from the label of the hybridization product, and

comparing the intensity of radiation at a time where a differential level of radiation emitted discriminate between a match and a mismatch.

44. The method for distinguishing a match and a mismatch between a target and a probe of claim 43 wherein the time is less than substantially 60 seconds.

45. A method for electronic perturbation catalysis of substrate molecules on an electronic control device containing at least one microlocation comprising the steps of:

immobilizing on the microlocation an arrangement of at least two catalytically reactive groups,

exposing the reactive groups to a solution containing the substrate molecules of interest, and applying an electronic pulsing sequence which causes separation between the two catalytic reactive groups to produce a catalytic reaction of the substrate molecules.

46. The method for electronic perturbation catalysis of substrate molecules of claim 45 wherein the reactive groups include cysteine (thiol) and histidine (imidazole) containing catalytic peptide sequence.

Heller '486

Likewise, claims 1-37 of Heller '486 (reproduced below) are silent regarding the aforementioned aspects (i) and (ii).

1. A method for hybridization analysis between a sample and a probe, the analysis utilizing an electronic stringency control device, comprising the steps of:

providing the sample and probe with a fluorescent label under hybridization conditions on the electronic stringency control device, forming a fluorescently labelled hybridization product,

monitoring the fluorescence from the hybridization product,

subjecting the hybridization product to varying electrophoretic force, and

analyzing the fluorescent signal from the flourescently labeled hybridization product for variance as a function of said varying electrophoretic force.

2. The method for hybridization analysis of claim 1 wherein the fluorescence is analyzed for the fluorescent perturbation value.

3. The method for hybridization analysis of claim 2 wherein the fluorescence perturbation value is measured for the onset value.

4. The method for hybridization analysis of claim 2 wherein the fluorescence perturbation value is measured for its height.

5. The method for hybridization analysis of claim 2 wherein the fluorescence perturbation value is measured for the slope.

6. The method for hybridization analysis of claim 1 wherein the fluorescence is analyzed for the power level of the perturbation.

7. The method for hybridization analysis of claim 1 further including the steps of:

determining a second measure of hybridization between the sample and the probe, and

combining the information obtained by the first analysis including the step of subjecting the hybridization product to the varying electrophoretic force in the second measure to provide a indication of hybridization.

8. The method for hybridization analysis of claim 7 wherein the second measure of hybridization includes determination of the electronic melting point.

9. The method for hybridization analysis of claim 1 wherein the fluorescent label is placed in proximity to the initial denaturation site.

10. The method for hybridization analysis of claims 1 or 9 wherein the fluorescent label is intercalated adjacent a single base mismatch site.

11. The method for hybridization analysis of claim 10 wherein the fluorescent label is ethidium bromide.

12. The method for hybridization analysis of claim 10 wherein the fluorescent label is acridine.

13. The method for hybridization analysis of claims 1 or 7 wherein the electrophoretic force is in an amount less than is necessary to effect dehybridization of the sample and the probe.

14. The method for hybridization analysis of claim 1 wherein the hybridization product is subject to an oscillating electrophoretic force.

15. The method for hybridization analysis of claim 7 wherein the fluorescent label is placed in proximity to the initial denaturation site.

16. The method for hybridization analysis of claim 13 wherein the electrophoretic force is in an amount less than is necessary to effect complete denaturation of the sample and the probe.

17. The method for hybridization analysis of claim 14 where the fluorescent signal from a mismatched sample and probe exhibits a relatively greater response to the oscillating electrophoretic force relative to a matched hybridization product.

18. The method for hybridization analysis of claim 1 wherein the probe is longer than a 20-mer.

19. The method for hybridization analysis of claim 1 further including the step of averaging of the fluorescent signal.

20. A method for hybridization analysis between a sample and a probe comprising the steps of:

providing the sample and probe with a fluorescent label under hybridization conditions, forming a fluorescently labeled hybridization product,

monitoring the fluorescence from the hybridization product,

subjecting the hybridization product to varying electrophoretic force, and

analyzing the fluorescent signal for variance as a function of said varying electrophoretic force to determine the fluorescence perturbation value.

21. The method for hybridization analysis of claim 20 wherein the fluorescence perturbation value is measured for the onset value.

22. The method for hybridization analysis of claim 20 wherein the fluorescence perturbation value is measured for its height.

23. The method for hybridization analysis of claim 20 wherein the fluorescence perturbation value is measured for the slope.

24. The method for hybridization analysis of claim 20

wherein the fluorescence is analyzed for the power level of the perturbation.

25. The method for hybridization analysis of claim 20 further including the steps of:

determining a second measure of hybridization between the sample and the probe, and

combining the information obtained by the first analysis including the step of subjecting the hybridization product to the varying electrophoretic force in the second measure to provide a indication of hybridization.

26. The method for hybridization analysis of claim 25 wherein the second measure of hybridization includes determination of the electronic melting point.

27. The method for hybridization analysis of claim 20 wherein the fluorescent label is placed in proximity to the initial denaturation site.

28. The method for hybridization analysis of claim 20 wherein the fluorescent label is intercalated adjacent a single based mismatch site.

29. The method for hybridization analysis of claims 27 or 28 wherein the fluorescent label is ethidium bromide.

30. The method for hybridization analysis of claims 27 or 28 wherein the fluorescent label is acridine.

31. The method for hybridization analysis of claim 20 wherein the electrophoretic force is in an amount less than is necessary to effect dehybridization of the sample and the probe.

32. The method for hybridization analysis of claim 20 wherein the hybridization product is subject to an oscillating electrophoretic force.

33. The method for hybridization analysis of claim 25 wherein the fluorescent label is placed in proximity to the initial denaturation site.

34. The method for hybridization analysis of claim 31 wherein the electrophoretic force is in an amount less than is necessary to effect complete denaturation of the sample and the probe.

35. The method for hybridization analysis of claim 32 where the fluorescent signal from a mismatch sample and probe exhibits a relatively greater response to the oscillating electrophoretic force relative to a matched hybridization product.

36. The method for hybridization analysis of claim 20 wherein the probe is longer than a 20-mer.

37. The method for hybridization analysis of claim 20 further including the step of averaging of the fluorescent signal.

Heller '696

Similarly, claims 1-46 of Heller '696 (reproduced below) do not disclose or suggest, for example, the aspect of (i) ***subjecting said individually selected microscopic locations to an electric field prior to hybridization*** and contacting said sample oligonucleotide sequence with said one or more anchor sequences thereby allowing said sample oligonucleotide sequence to hybridize to said one or more anchor (independent claim 49).

1. A method for electronically controlling nucleic acid hybridization, comprising the steps of:
connecting multiple locations to an electrical source;
contacting a plurality of specific nucleic acids with target nucleic acids, wherein said specific nucleic acids are attached to said locations; and
placing at least one of said locations at a negative potential for a sufficient time, wherein a non-specific nucleic acid sequence to said target nucleic acid but not a specific nucleic acid sequence from said plurality of nucleic acids is removed from said target nucleic acid.

2. A method for electronically controlling hybridization of DNA from a solution containing specific binding and non-specific binding DNA sequences to a binding location, comprising the steps of:
placing the solution in contact, under suitable conditions such that hybridization is permitted, with a first binding location including a first underlying

electrode, and a second binding location including a second underlying electrode;

placing said first binding location at a positive potential, relative to said second binding location, concentrating DNA on said first location surface; and

placing said first binding location at a negative potential, relative to said second binding location, wherein said negative potential or current is sufficient to remove the non-specifically bound DNA sequences from said first binding location, but not sufficient to remove the specifically bound DNA sequences.

3. A method for electronically controlling hybridization of DNA from a solution containing specific binding and non-specific binding DNA sequences to first and second binding locations, comprising the steps of:

placing the solution in contact, under suitable conditions such that hybridization is permitted, with the first, second, and a third locations;

placing said first and second binding locations at a positive potential and said third location at a negative potential, concentrating DNA on said first and second locations;

placing said first and second specific binding locations at a negative potential and said third location at a positive potential; and

placing said first and second binding locations at negative potentials, relative to said third location, wherein said negative potential or current is sufficient to remove the non-specifically bound DNA from said first and second locations, but not sufficient to remove the specifically bound DNA sequences.

4. A method for electronically controlling hybridization of DNA from a solution containing specific and non-specific DNA sequences to a first binding location and then to a second specific binding location, comprising the steps of:

placing the solution in contact, under suitable conditions such that hybridization is permitted, with said first, second, and a third location;

placing said first binding location at a positive potential and said second binding location at a negative potential, concentrating DNA on said first location;

placing said first binding location at a negative potential and said second binding location at a positive potential, concentrating DNA on said second location; and

placing said first and second binding locations at

negative potentials, relative to said third binding location, wherein said negative potential or current is sufficient to remove the non-specifically bound DNA from said first and second locations but not sufficient to remove the specifically bound DNA.

5. The method of hybridization of claims 2, 3, or 4 wherein said negative potential or current is increased or decreased incrementally.

6. The method of claims 2, 3, or 4 wherein multiple specific and non-specific DNA sequences are applied to an array of binding locations.

7. A method for stringency control in the multiple-site, array based analysis of the hybridization state of nucleic acids, the improvement comprising the use of electrophoretic potential as a stringency condition.

8. The method of claim 7 wherein temperature is additionally used as a stringency condition.

9. The method of claims 7 or 8 wherein the salt condition is additionally used as a stringency condition.

10. The method of claim 7 wherein the constitution of the buffer is additionally used as a stringency condition.

11. The method of claim 7 wherein pH is additionally used as a stringency condition.

12. The method of claim 7 wherein the method affects resolution of single basepair mismatches in five minutes or less.

13. The method of claim 7 wherein different stringency conditions can be applied at different sites in the array.

14. The method of claim 7 wherein different stringency conditions can be applied at multiple sites in the array at the same time.

15. A method for independent stringency control in the multiple-site, array based analysis of the hybridization state of nucleic acids, the improvement comprising the use of electrophoretic potential as a stringency condition which differs at various sites at the same time.

16. The method of claim 15 wherein temperature is additionally used as a stringency condition.

17. The method of claims 15 or 16 wherein salt condition is additionally used as a stringency condition.

18. The method of claim 15 wherein the constitution of the buffer is additionally used as a stringency condition.

19. The method of claim 15 wherein pH is additionally used as a stringency condition.

20. The method of claim 15 wherein the method affects resolution of single basepair mismatches in five minutes or less.

21. A method for electronically controlling binding between macromolecules, comprising the steps of:

contacting, under suitable conditions such that binding is permitted, a charged first macromolecule with a second macromolecule in a region spaced apart from an electrode by a permeation layer,

operating the electrode in a manner to apply a signal which varies in time sequence in both magnitude and sign to cause an electrically repulsive force on at least the charged first macromolecule so as to determine the state of binding between the first macromolecule and second macromolecule, and

detecting the state of binding between the first macromolecule and second macromolecule.

22. The method for electronically controlling binding between macromolecules of claim 21 further including the step of actively transporting the charged first macromolecules to the said region.

23. The method for electronically controlling binding between macromolecules of claim 22 wherein the step of actively transporting the charged first macromolecule is affected by applying an attractive potential to the electrode.

24. The method for electronically controlling binding between macromolecules of claim 23 wherein the attractive potential is a positive potential.

25. The method for electronically controlling binding between macromolecules of claim 22 wherein the step of

actively transporting the charged first macromolecule is affected by the use of an attractive electrophoretic force.

26. The method for electronically controlling binding between macromolecules of claim 21 wherein the contacting of the charged first macromolecule with a second macromolecule in the region is aided by electronically enhanced interaction.

27. The method for electronically controlling binding between macromolecules of claim 26 wherein the electronically enhanced interaction concentrates the charged first macromolecule within the region.

28. The method for electronically controlling binding between macromolecules of claim 23 wherein the electrically repulsive force constitutes a potential which is a reversal of the attractive potential previously applied to the electrode.

29. The method for electronically controlling binding between macromolecules of claim 21 wherein the electrically repulsive force constitutes a constant current.

30. The method for electronically controlling binding between macromolecules of claim 21 wherein the electrically repulsive force constitutes a constant voltage.

31. The method for electronically controlling binding between macromolecules of claim 21 wherein the electrically repulsive force constitutes a defined power level.

32. The method for electronically controlling binding between macromolecules of claim 21 further including the step of electronically removing non-specifically bound materials.

33. The method for electronically controlling binding between macromolecules of claim 21 wherein the step of operating the electrode in a manner to cause an electrically repulsive force on at least the charged first macromolecule so as to determine the state of binding between the first macromolecule and second macromolecule, the repulsive force removes the non-complementary macromolecules but does not remove the complementary macromolecules.

34. The method for electronically controlling binding between macromolecules of claim 21 wherein the step of

detecting is performed optically.

35. The method for electronically controlling binding between macromolecules of claim 34 wherein the step of optical detecting is fluorescent detection.

36. The method for electronically controlling binding between macromolecules of claim 35 wherein the step of optical fluorescence detecting utilized dyes which bind to DNA.

37. The method for electronically controlling binding between macromolecules of claim 36 wherein the dyes possess a differential affinity for double stranded DNA relative to single stranded DNA.

38. The method for electronically controlling binding between macromolecules of claim 36 wherein the step of optical fluorescence detecting utilizes charged dyes.

39. The method for electronically controlling binding between macromolecules of claim 38 wherein the charged dyes are removed from unhybridized DNA by application of power.

40. The method for electronically controlling binding between macromolecules of claim 34 wherein the step of optical detecting is spectrophotometric detection.

41. The method for electronically controlling binding between macromolecules of claim 21 further including a plurality of electrodes, the electrodes being operable in a manner to cause an different electrically repulsive forces at the various electrodes.

42. A method for improved stringency control of nucleic acid hybridization reactions comprising the steps of:

transporting reactants or analytes to a microlocation containing attached specific binding entities,

concentrating the reactants or analytes at one or more specific microlocations where hybridization may occur with the specific binding entities,

selectively removing unreacted and non-specifically bound components from microlocations where hybridization has occurred by raising the electric potential,

varying the repulsive force by applying a signal which varies in time sequence in both magnitude and sign at the microlocation so as to vary the detectable characteristic of the microlocation, and

detecting the state of hybridization.

43. The method for improved stringency control of claim 42 further including the step of adjusting the electric potential to improve the resolution of single basepair mismatched hybridizations.

44. The method for improved stringency control of claim 43 wherein the single basepair mismatch hybridizations identify point mutations.

45. The method for improved stringency control of claim 42 further including the step of applying independent electric potential control to individual hybridization events occurring in the same bulk solution.

46. The method for improved stringency control of claim 42 further including the step of using electric potential control to improve hybridization of unamplified target DNA sequences to arrays of capture oligonucleotide probes.

Sosnowski '421

Further, claims 1-8 of Sosnowski '421 (reproduced below) say nothing regarding (i) ***subjecting said individually selected microscopic locations to an electric field prior to hybridization*** and contacting said sample oligonucleotide sequence with said one or more anchor sequences thereby allowing said sample oligonucleotide sequence to hybridize to said one or more anchor (independent claim 49), and (ii) forming a plurality of individually electronically addressable microscopic locations on a substrate, each microscopic location comprising a micro-electrode, and ***said sample oligonucleotide sequence is free to move and be transported between said microscopic locations on said substrate*** (independent claim 82)

1. A method for detecting a single nucleotide polymorphism in a sample nucleic acid using an electronically addressable microchip having a plurality of test sites, wherein each of the test sites comprises an individually controllable electrode covered by a permeation layer, the method comprising:

providing a sample nucleic acid suspected of containing a single nucleotide polymorphism;

electronically biasing the sample nucleic acid to a test site of the plurality of test sites on the microchip, and concentrating the sample nucleic acid at the test site;

immobilizing the sample nucleic acid onto the test site;

electronically hybridizing a mixture comprising a first probe with a label selected from the group consisting of fluorescent label, colorimetric label, and chemiluminescent label, and a second probe with a label selected from the group consisting of fluorescent label, colorimetric label, and chemiluminescent label to the sample nucleic acid , wherein the first probe is perfectly complementary to the sample nucleic acid and contains a nucleotide perfectly complementary to the nucleotide at the site of the polymorphism, and forms a first hybridized complex, and the second probe is complementary to the sample nucleic acid and contains a nucleotide which forms a mismatch with the nucleotide at the site of the polymorphism, and forms a second hybridized complex, wherein the label of the first probe and the label of the second probe are different;

subjecting the first and second hybridized complexes to destabilizing conditions sufficient to cause the first probe to dissociate from the first hybridized complex or the second probe to dissociate from the second hybridized complex if there is at least one base-pair mismatch between the first probe or the second probe and the sample nucleic acid; and

detecting the first or second hybridized complex following the subjecting step by determining a signal intensity from the label of the first probe of the first hybridized complex or a signal intensity from the label of the second probe of the second hybridized complex, wherein the single nucleotide polymorphism in the sample nucleic acid is detected if the signal intensity from the label of the first probe of the first hybridized complex is present.

2. The method of claim 1, further comprising the step of subjecting the sample nucleic acid to an amplification reaction before said biasing step.

3. The method of claim 1, wherein the sample nucleic acid further comprises a biotin moiety, and wherein the sample nucleic acid is immobilized onto the test site by a biotin-streptavidin interaction.

4. The method of claim 1, wherein the label of the first probe and the label of the second probe are different fluorophores.

5. The method of claim 4, wherein the different fluorophores are selected from the group consisting of Cy3 and Cy5.

6. The method of claim 1, further comprising the steps of:

providing another sample nucleic acid containing the single nucleotide polymorphism;

electronically biasing the another sample nucleic acid to an another test site of the plurality of test sites on the microchip, concentrating the another sample nucleic acid at the another test site; and

immobilizing the another sample nucleic acid onto the another test site.

7. The method of claim 1, wherein the hybridization step is repeated with at least one additional mixture of the first and second probes.

8. The method of claim 1, wherein the hybridization step is performed under electronic stringency conditions.

Applicant submits that the cited references (including Cozzette), even when considered along with common sense and common knowledge to one skilled in the art, simply does ***NOT*** render unpatentable the aspect of claim 49 of the present application (i) ***subjecting said individually selected microscopic locations to an electric field prior to hybridization*** and contacting said sample oligonucleotide sequence with said one or more anchor sequences thereby allowing said sample oligonucleotide sequence to hybridize to said one or more anchor, nor the aspect of claim 82 of the present application of (ii) forming a plurality of individually electronically addressable microscopic locations on a substrate, each microscopic location comprising a micro-electrode, and ***said sample oligonucleotide sequence is free to move and be transported between said microscopic locations on***

said substrate.

In view of the remarks hereinabove, applicant maintains that the application is now allowable, and applicant earnestly solicits the allowance of the application.

However, if the Examiner can suggest an amendment that would advance this application to condition for allowance, the Examiner is respectfully requested to call the undersigned attorneys.

If a petition for an extension of time is required to make this response timely, this paper should be considered to be such a petition.

No fee is deemed necessary in connection with the filing of this Amendment. However, if any further fees are required, authorization is hereby given to charge the amount of any such required fee to Deposit Account No. 03-3125.

Respectfully submitted,

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Date